

GTCAAGGAAGAGGTACCTGGTGTCCATCAAGGTGCAGTCGGCCGGCATGACCAAGTG  
 AGGTGGTTGAAGATAGCACCATCACCATGATAGACCGCCCGCCTCAACCGCCTCCA  
 CACATCCGTGTGAATGAAAAGGATGTGCTAATCAGCAAATCTTCCATCAACTTTACT  
 GTCAACTGCAGCTGGTTCAGCGACACCAACGGAGCGGTTGGGTACTTTGCTGTGGTG  
 GTGAGAGAGGCCGACAGCATGGATGAGTTGAAGCCAGAACAGCAGCACCCTCTCCC  
 TTCCTACCTGGAGTACAGACACAACGCCTCCATCCGAGTCTACCAGACCAATTATTT  
 TGCCAGCAAATGTGCTGAAAGTCCCGACAGCAGTTCTAAAAGTTTCAACATTAAGCT  
 TGGAGCAGAGATGGACAGCCTCGGTGGCAAATGTGATCCCAGTCAGCAGAAATTCT  
 GTGATGGACCGCTGTTGCCACACACCGCCTACAGAATCAGCATCCGGGGCTTTTACAC  
 AGCTATTTGACGAGGACTTGAAAGAGTTACCAAACCTCTCTACTCGGATACGTTCT  
 TCTCTATGCCCATCACCACAGAGTCAGAGCCCTTGTTTGGAGTTATTGAAGGTGTGA  
 GTGCTGGCCTGTTTCTAATTGGCATGCTGGTGGCCCTTGTTGCCTTCTTCATCTGCAG  
 ACAGAAAGCTAGCCACAGCAGGGAAAGGCCATCTGCCCGGCTCAGCATTTCGTAGGG  
 ACCGGCCTTTGTCTGTCCATCTGAATCTGGGCCAGAAAGGCAACCGGAAAACCTTCTT  
 GCCCCATAAAGATCAATCAGTTTGAAGGGCATTTCATGAAGCTGCAGGCAGACTCC  
 AACTACCTTCTATCCAAGGAATATGAGGACTTAAAAGACGTGGGTAGAAGCCAGTC  
 ATGTGACATTGCCCTCTTGCCCTGAGAATCGAGGGAAAAATCGATACAACAACATATT  
 GCCTTATGATGCCTCAAGAGTGAAGCTCTCGAATGTCGATGACGACCCTTGCTCTGA  
 CTACATCAACGCCAGCTACATCCCCGGTAACAACCTTCAGACGAGAATACATCGCCA  
 CTCAGGGACCGCTTCCAGGCACCAAGGATGACTTCTGGAAGATGGCGTGGGAGCAG  
 AACGTTCAACAACATCGTCATGGTGACCCAGTGTGTTGAAAAGGGCCGAGTGAAGTG  
 TGACCATTACTGGCCAGCAGACCAGGACCCCCCTCTACTACGGTGATCTCATCCTACA  
 GATGGTCTCGGAGTCCGTGCTCCCCGAGTGGACCATCAGGGAGTTTAAGATATGCAG  
 TGAAGAACAGTTGGATGCACACAGACTCATCCGTCACCTTCACTACACGGTGTGGCC  
 AGACCATGGGGTCCCAGAGACCACCCAGTCCCTGATCCAATTTGTGAGGACAGTCA  
 GGGACTACATCAACAGAAGCCCCGGGGCTGGGCCCTCCGTAGTGCAGTGCAGCGCT  
 GGTGTGGGCAGAACAGGGACGTTGTTGCCCTGGACCGGATCCTCCAGCAGTTGGA  
 CTCTAAGGACTCCGTGGACATTTATGGGGCAGTGCATGACCTAAGACTCCACAGGGT  
 TCACATGGTCCAGACCGAGTGTCAATATGTGTATCTGCATCAGTGTGTAAGAGACGT  
 CTCAGAGCAAAGAACTGCGGAAACGAGCAAGAGAAAGGGGGTGTTCGATTTATG  
 AGAATGTGAATCAGAGTATCACAGAGATGCAATCTACTCGAGACATTAAGAATTC  
 (SEQ ID NO:1)

**FIGURE 1**

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

[GTCAAGGAAGAGGTACCTGGTGTCCATCAAGGTGCAGTCG] GCCGGCATGACCAGTGAGGT  
 GGTGAAGATAGCACCATCACCATGATAGACCGCCCGCCTCAACCGCCTCCACACATCCG  
TGTGAATGAAAAGGATGTGCTAATCAGCAAATCTTCCATCAACTTTACTGTCAACTGCAG  
CTGGTTCAGCGACACCAACGGAGCGGTTGGGTACTTTGCTGTGGTGGTGAGAGAGGCCGA  
CAGCAT [GGATGAGTTGAAGCCAGAACAGCAGCACCCTCTCCCTTCCTACCTGGAGTACAG  
 ACACAACGCCTCCATCCGAGTCTACCAGACCAATTATTTGCCAGCAAATGTGCTGAAAG  
 TCCCGACAGCAGTTCTAAAAGTTTCAACATTAAGCTTGGAGCAGAGATGGACAGCCTCGG  
 TGGCAAATGTGATCCCGAGTCAGCAGAAATTCTGTGATGGACCGCTGTTGCCACACACCGC  
 CTACAG] AATCAGCATCCGGGCTTTTACACAGCTATTTGACGAGGACTTGAAAGAGTTTAC  
 CAAACCTCTCTACTCGGATACGTTCTTCTCTATGCCCATCACCACAGAGTCAGAGCCCTT  
 GTTTGGAGTTATTGAAGGTGTGAGTGCTGGCCTGTTTCTAATTGGCATGCTGGTGGCCCT  
 TGTTGCCCTTCTTCATCTGCAGACAGAAAGCTAGCCACAGCAGGGAAAGGCCATCTGCCCG  
 GCTCAGCATTCTGATGGGACCGGCCTTTGTCTGTCCATCTGAATCTGGGCCAGAAAGGCAA  
 CCGGAAAACCTTCTTGCCCCATAAAGATCAATCAGTTTGAAGGGCATTTCATGAAGCTGCA  
 GGCAGACTCCAACCTACCTTCTATCCAAGGAATATGAGGACTTAAAAGACGTGGGTAGAAG  
 CCAGTCATGTGACATTGCCCTCTTGCTGAGAATCGAGGGAAAAATCGATACAACAACAT  
 ATTGCCCTTATGATGCCTCAAGAGTGAAGCTCTCGAATGTGATGACGACCCCTTGCTCTGA  
 CTACATCAACGCCAGCTACATCCCCGGTAACAACCTCAGACGAGAATACATCGCCACTCA  
 GGGACCGCTTCCAGGCACCAAGGATGACTTCTGGAAGATGGCGTGGGAGCAGAACGTTCA  
 CAACATCGTCATGGTGACCCAGTGTGTTGAAAAGGGCCGAGTGAAGTGTGACCATTACTG  
 GCCAGCAGACCAGGACCCCTCTACTACGGTGATCTCATCCTACAGATGGTCTCGGAGTC  
 CGTGCTCCCCGAGTGGACCATCAGGGAGTTTAAGATATGCAGTGAAGAACAGTTGGATGC  
 ACACAGACTCATCCGTCACCTTCTACTACACGGTGTGGCCAGACCATGGGGTCCCAGAGAC  
 CACCCAGTCCCTGATCCAATTTGTGAGGACAGTCAGGGACTACATCAACAGAAGCCCCGG  
 GGCTGGGCCCTCCGTAGTGCACTGCAGCGCTGGTGTGGGCAGAACAGGGACGTTCTGTTGC  
 CCTGGACCGGATCCTCCAGCAGTTGGACTCTAAGGACTCCGTGGACATTTATGGGGCAGT  
 GCATGACCTAAGACTCCACAGGGTTTACATGGTCCAGACCGAGTGTCAATATGTGTATCT  
 GCATCAGTGTGTAAGAGACGTCTCAGAGCAAAGAACTGCGGAAACGAGCAAGAGAAAGG  
 GGGTGTTCGATTTATGAGAATGTGAATCAGAGTATCACAGAGATGCAATCTACTCGAGA  
 CATTAAGAATTC

**FIGURE 2A**

# Gene Sequence Structure \*

41 bp

Sequence Deleted

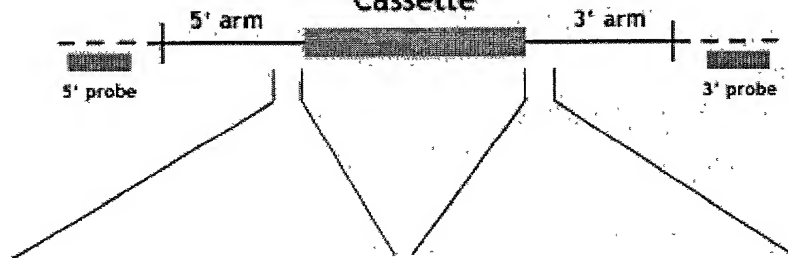
246 bp

Size of partial cDNA: 1752 bp



## Targeting Vector\* (genomic sequence)

### LacZ-Neo Cassette



Arm Length:  
5': 0.7 kb  
3': 2.5 kb

5'>GCCGCCCCCAGAACTCCACGG  
CCATTGCCTGCTCTTGGATACCTC  
CTGACTCCGACTTTGATGGCTACA  
GCATTGAGTGCCGAAAAATGGATA  
CCCAAGAAATCGAGTTTCCAGAA  
AGCTGGAGAAAGAAAAATCACTGC  
TCAACATCATGATGTTAGTACCTC  
ATAAGAGGTACCTGGTGTCCATCA  
AGGTGCAGTCG<3'  
(SEQ ID NO:2)

5'>GGATGAGTTGAAGCCAGAACA  
GCAGCACCTCTCCCTTCCTACCT  
GGAGTACAGACACAACGCCTCCAT  
CCGAGTCTACCAGACCAATTATTT  
TGCCAGCAAATGTGCTGAAAGTCC  
CGACAGCAGTTCTAAAAGTTTCAA  
CATTAAGCTTGGAGCAGAGATGGA  
CAGCCTCGGTGGCAAATGTGATCC  
CAGTCAGCAGA<3'  
(SEQ ID NO:3)

———— Targeting Vector  
- - - - Endogenous Locus

\* Not drawn to scale

FIGURE 2B